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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.

EXAMINER	
ART UNIT	PAPER NUMBER

DATE MAILED:

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/254,529	Kingsman et al
Examiner	**Group Art Unit**
SUMESH KAUSHAL	1633

X Responsive to communication(s) filed on *May 19, 2000*

This action is **FINAL.**

Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claim

X Claim(s) *1-18* is/are pending in the applicat

Of the above, claim(s) _____ is/are withdrawn from consideration

Claim(s) _____ is/are allowed.

X Claim(s) *1-18* is/are rejected.

Claim(s) _____ is/are objected to.

Claims _____ are subject to restriction or election requirement.

Application Papers

See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

The drawing(s) filed on _____ is/are objected to by the Examiner.

The proposed drawing correction, filed on _____ is approved disapproved.

The specification is objected to by the Examiner.

The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

All Some* None of the CERTIFIED copies of the priority documents have been

received.

received in Application No. (Series Code/Serial Number) _____.

received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

X Notice of References Cited, PTO-892

X Information Disclosure Statement(s), PTO-1449, Paper No(s). *7*

Interview Summary, PTO-413

Notice of Draftsperson's Patent Drawing Review, PTO-948

Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

The applicant's response filed on Paper No. 8, 05/19/00 has been fully considered but they are not persuasive for the reasons set forth in the earlier office action mailed 02/15/00

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 U.S.C. § 112

1. Claims 15-16 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for inserting a selected gene into a target cell in vitro using a retroviral viral vector, does not reasonably provide enablement for any method for inserting a selected gene into target cells in vivo using a retroviral vector. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to the invention **commensurate in scope** with these claims.

2. Applicant's arguments filed 05/19/00, page 3 have been fully considered but they are not persuasive. The applicant argues that claim has been amended to recite a method for inserting a selected gene into a target cell by contacting the target cell with the retroviral vector.

However, this is found not persuasive because the method as claimed read upon in vivo gene delivery using the retroviral vector which fall in the realm of gene therapy. The Official action mailed on 2/15/00 clearly states that gene therapy is an unpredictable art because it had been difficult to predict the transduction efficiency and out come of transduced therapeutic genes (Anderson WF,

Nature 392:25-30, 1998). The art at the time of filing teaches that various factors govern the expression and/or therapeutic potential of transduced genes in vivo. The transduction of appropriate target cells represents the first critical step in vivo gene delivery which depends upon the choice and design of a vector used. Retroviral vectors require target cells to be in cycling state at the time of infection for the successful delivery of transgenes. Moreover, the requirements of in vivo gene delivery systems are quite demanding, besides limitations in gene transfer the problem to selectively target cells is still one of the most difficult obstacle to overcome. The viral particles binds to many cells they encounter in vivo and therefor would be diluted out before reaching their targets (Anderson WF, page 25 col.2, para.4). Furthermore, in vitro gene transfer studies are not predictive of in vivo gene therapy because gene transfer frequency is much higher with in-vitro models where most of cells are under going rapid cell division, which is clearly not the case in vivo. Although, gene therapy may become powerful technology, it is still in the state of development which render the art of gene therapy unpredictable due to the lack of basic understanding of a vector design and its interaction with host cells (Anderson WF, page 30 col.1, para. 5).

Thus, in view of lack of specific guidance in the specification and considering the state of art, the skilled artisan at the time of filing would be unable to use the claimed invention, without an excessive and undue amount of experimentation. The quantity of experimentation required to practice the invention as claimed would include successful delivery of a selected gene and it's expression into a target cell in vivo, using any and all retroviral vectors.

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) a patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. Claims 1-14 and 17-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cohli et al (Antisense Res. and Dev. 4:19-26, 1994), Naldini et al (Science 272:263-267, 1996.), Hope et al (PNAS, 87:7787-7791, 1990) and Lisziewicz (WO92/21750, 1992).

Cohli et al teaches retroviral vectors (MoMuLV) expressing HIV-1 packaging signal and REV response element (RRE) in sense or antisense orientation wherein the RRE sequence are expressed under the control of HSV-tk promoter fused to HIV TAR element, while the packaging signal sequence are expressed under the control of HSV-tk promoter. Cohli et al further teaches that both RRE and packaging signal sequences are expressed as part of 3' untranslated region of NEO gene (page 19, abstract, page 23, fig-1).

However, Cohli et al does not teaches a retroviral vector, wherein the vector contains splice donor sequence, RRE and splice acceptor sequences, and the expression of the gene of interest is driven by internal promotor (CMV). Furthermore, Cohli et al does not teaches a retroviral vector wherein the gene of interest is located within an intron in a transciprion unit of the provirus.

Naldini et al teaches a three plasmid retroviral expression system wherein the transfer vector comprising splice donor sequence, RRE and splice acceptor sequences (page 263, fig-1) Naldini et al further teaches the use of internal promotor CMV to drive the expression of a gene of interest (page 263, fig-1).

Hope et al teaches that HIV-1 transactivator Rev is a nuclear protein that regulates the expression of HIV transcripts by binding to the Rev response elements (RRE) present in the HIV transcripts. Hope et al further teaches a retroviral vector comprising splice donor sequence, RRE and splice acceptor sequences, wherein the gene of interest (CAT) is located within the splice donor and splice acceptor site (page 7787, abstract; page 7788, fig-1).

Liziewicz teaches a retroviral vector incorporating Rev/RRE system, wherein the RRE or functional equivalent thereof is located within the transcriptional unit of the foreign gene or within the transcriptional unit of the vector (page 6, line 21-32 page 9, line 1-4 and fig. 1-4). Liziewicz further teaches that the vector contain an internal promoters operably linked to the foreign gene and DNA sequence encoding the RRE (page 9, line 5-26).

Thus it would have been obvious to one ordinary skill in the art at the time of filing to modify the retroviral vector as taught by Cohli et al with the insertion of splice donor sequence, RRE and splice acceptor sequences wherein the expression of the gene of interest is regulated by an internal promotor (CMV) as taught bu Naldini et al. It would have been further obvious to modify the teaching of Cohli and Naldni et al by inserting the gene of interest within the splice acceptor site as taught by Hope et al. In addition, it would have been further obvious to modify the retroviral vector as taught by Cohli, Hope and Naldni with the insertion RRE element into the intron of the foreign gene contained within the vector. One would have been motivated to do so because the insertion of a RRE into the intron of foreign gene and with in splice donor and splice acceptor sites provides the regulation of the expression of a foreign gene by RRE element.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sumesh Kaushal Ph.D. whose telephone number is (703) 305-6838. The examiner can normally be reached on Monday-Friday from 8:30 AM to 4:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Deborah Clark can be reached on (703) 305-4051. The fax phone number for the organization where this application or proceeding is assigned as (703) 308-4242. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the group receptionist whose telephone number is (703) 308-0196.

S. Kaushal, AU 1633

DEBORAH J.R. CLARK
PRIMARY EXAMINER